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Page 1 of 1

Docket No.: MANNK.021CP1C

CUSTOMER NO. 20995

Applicant : Simard, et al.
App. No. : 10/026,066
Filed : December 7, 2001
For : EPI TOPE SYNCHRONIZATION
ANTIGEN PRESENTING CELLS
Examiner : VanderVegt, Francois P.
Group Art Unit : 1644

IN

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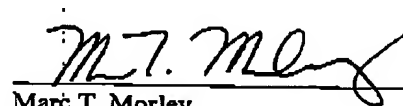
July 25, 2006


Marc T. Morley, Reg. No. 52,051

Transmitted herewith for filing and consideration in the above-referenced application are the following items:

- (X) Pre-Appeal Brief Request for Review in six (6) pages.
- (X) Notice of Appeal in two (2) page.
- (X) Total pages in transmission: 9

The Commissioner is hereby authorized to charge any additional fees which may be required, now or in the future, or credit any overpayment to Account No. 11-1410.


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JUL 25 2006

MANNK.021CP1C

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Simard et al.
Appl. No. : 10/026,066
Filed : December 7, 2001
For : EPITOPE SYNCHRONIZATION
IN ANTIGEN PRESENTING
CELLS
Examiner : VanderVegt, Francois P.
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Marc T. Morley, Reg. No. 52,051

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicants request review of the final rejection in the above-identified application. No
amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reasons stated in the accompanying Remarks, which begin
on page 2 of this paper.

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REMARKS

Applicants request pre-appeal brief review of the sole remaining rejection in the above-referenced application, namely the written description rejection of all of the pending claims under 35 U.S.C. § 112, first paragraph.

Concise Statement of Reasons for Review

Claims 1-5, 29-37 and 38-57 are pending in the application, with Claims 1 and 42 being the only independent claims. Claims 1 and 42 recite, respectively:

1. (Previously presented) A composition suitable for adoptive administration to a human, comprising a first isolated T cell in a pharmaceutically acceptable formulation suitable for adoptive administration to a human, the formulation comprising a pharmaceutically acceptable carrier, adjuvant, diluent, or excipient, wherein said T cell expresses a T cell receptor specific for an MHC-peptide complex comprising a first housekeeping epitope, wherein the housekeeping epitope is derived from a first antigen associated with a first target cell.

42. A composition suitable for adoptive administration to an animal, comprising at least a first and a second isolated T cell population, wherein said first population expresses a T cell receptor specific for a first MHC-peptide complex comprising a first housekeeping epitope derived from a first antigen associated with a first target cell, and wherein said second population expresses a T cell receptor specific for a second MHC-peptide complex comprising a second housekeeping epitope derived from a second antigen associated with a second target cell, wherein the first housekeeping epitope and the second housekeeping epitope are not the same.

Applicants respectfully submit that written description requirement is satisfied because the recited compositions of Claims 1 and 42 are described in sufficient detail that one of skill in the relevant art could conclude that the inventors were in possession of the claimed invention at the time the application was filed. *See Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, (Fed. Cir. 1991). As two specific examples, Applicants submit that (1) the specification fully describes adoptive administration and isolated T cells that express a T cell receptor specific for an MHC-peptide complex comprising a housekeeping epitope and (2) the specification describes the genus of housekeeping epitopes.

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Adoptive Administration and Isolated T cells are Fully Described

Adoptive therapy with T cells is described on pages 107 and 108 of the application as filed. In particular, pages 107 and 108 describe how to obtain, isolate and expand suitable T cells, including T cells that can recognize housekeeping and/or other epitopes. Furthermore, the specification describes how to test to verify that a given T cell expresses a T cell receptor specific for an MHC-peptide complex comprising a first housekeeping epitope, which permits one of skill in the art to distinguish members of the claimed genus. The Examples in the specification also describe various T cell assays methods to determine reactivity against housekeeping epitopes. Further discussion related to the description of T cells is found in the *Amendment and Response to Office Action* filed on November 3, 2005 ("November 3rd Response") at page 9 and in the *Response to Final Office Action* mailed on March 27, 2006 ("March 27th Response") at pages 14-15.

Description of Housekeeping Epitopes

Housekeeping epitopes are fully described as discussed in detail in the *November 3rd Response* at pages 7-9, and in the *March 27th Response* at pages 5-15 (and the Declaration of Dr. Adrian Bot filed with the *Response*).

For at least the above-mentioned reasons, Applicants submit that the written description requirement has been satisfied because the claimed subject matter has been fully described such that one of skill in the art would recognize that Applicants possessed the claimed subject matter at the time of filing the application.

Response to Examiner's Arguments

In the Final Office Action mailed on January 25, 2006, the Examiner made various assertions in connection with the written description rejection and dismisses Applicants' prior arguments as unpersuasive. In particular, the Examiner asserted that the "instant specification ... has described only several housekeeping epitopes from seven cancer-related proteins." The Examiner argued that "[t]he specification fails to describe any structural properties that are

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shared between housekeeping epitopes, only that they are processed by standard proteasomes, not immunoproteasomes."

The Examiner also argued that "[b]ecause there is no disclosure of any actual structural difference between housekeeping and immune epitopes, there is no reason to believe that a T cell which binds to a discovered housekeeping epitope cannot also bind an immuno-epitope with a related set of anchor residues."

In the Advisory Action mailed on June 2, 2006 the Examiner stated that Applicants' arguments in the response to the Final Office Action relate to the novelty of the housekeeping epitopes themselves. The Examiner further argued that there is no difference in the T cells that recognize housekeeping epitopes from T cells that recognize epitopes processed by immunoproteasomes. According to the Examiner, the epitopes recognized are the same, with the only difference being the manner in which an epitope is liberated from the larger polypeptide in which it is present. Thus, the examiner stated that the "claims are drawn to the use of the T cells in methods of treatment, not to the use of the housekeeping epitopes themselves."

Applicants' arguments regarding the description of housekeeping epitopes, including their distinguishing characteristics, are incorporated herein. Specifically, Applicants direct the Patent Office's attention to the *November 3rd Response* at pages 7-9 and to the *March 27th Response* at pages 6-15. The Declaration of Dr. Bot submitted with the *March 27th Response* indicates that housekeeping epitopes are a meaningful class of epitopes that can be distinguished from non-housekeeping epitopes, and that based upon the disclosure of the instant application, one of skill in the art would recognize that Applicants possessed the class of housekeeping epitopes at the time of filing the application. See *March 27th Response* at pages 6-15. Dr. Bot also explained that there are structural differences between housekeeping and non-housekeeping epitopes, and that functional characteristics of housekeeping and non-housekeeping epitopes serve as a proxy for their distinguishable structures due to the correlation between structure and function. See *Declaration of Dr. Bot*, for example, at page 4, paragraph 5D-5F.

With regard to the Examiner's arguments regarding the written description of T cells, Applicants again direct the Patent Office's attention to the *November 3rd Response* at page 9 and to the *March 27th Response* at pages 14-15. Furthermore, Applicants submit that whether there

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are structural similarities between certain housekeeping epitopes and certain immune epitopes, and whether some epitopes are liberated by the housekeeping and immune proteasomes is irrelevant to the written description of the instant claims. Also, the statements in the Advisory Action that the epitopes recognized by the T cells are the same, with the only difference being the manner in which an epitope is liberated, is factually incorrect. Although, there may be some epitopes liberated in nature by both proteasomes, there are many that are not, and generally, the epitopes and populations of epitopes liberated by the different proteasomes are distinct. Therefore, it appears that the examiner has based the rejection on a factually incorrect understanding of the art.

Applicants emphasize that the specification describes how to distinguish between housekeeping epitopes and non-housekeeping epitopes (epitopes not liberated by the housekeeping proteasome) and how to distinguish T cells that recognize those respective classes of epitopes. Finally, as set forth in the Declaration of Dr. Bot at pages 7-8, "a person of ordinary skill in the art would readily be able to make use of the recited diagnostic features in distinguishing between members and non-members of the genus of housekeeping epitopes. Because a particular T-cell receptor is specific for a particular target, a person of ordinary skill in the art would be able to distinguish the T-cells of the claimed compositions from other T-cells based on the description of housekeeping epitopes provided by the applicants."

Conclusion

For the reasons set forth above, Applicants submit that the pending claims comply with the written description requirement of 35 U.S.C. 112, first paragraph. The compositions comprising, *inter alia*, isolated T cells that express a T cell receptor specific for an MHC-peptide complex comprising a housekeeping epitope are described in such a way that one of skill in the art would recognize their possession by Applicants at the time of filing the application. With all due respect, Applicants have rebutted the arguments of record put forth by the Patent Office, including by providing a declaration by one of skill in the art.

Therefore, Applicants request withdrawal of the instant written description rejection and allowance of the pending claims.

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Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: July 25, 2006

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